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IN THE MATTER OF:

REINER ET AL.

GROUP: 1623

SERIAL NO. 09/524,757

EXAMINER: OWENS, H.

FILED: MARCH 14, 2000

FOR: PHARMACEUTICAL COMPOSITIONS BASED ON DICLOFENAC

DECLARATION UNDER 37 CFR 1.132

Hon. Commissioner of Patents
& Trademarks
Washington, DC 20231

SIR:

1) I, Alberto Reiner, am one of the inventors of the US Patent Application n. 09/524,757.

2) My background and a list of my published scientific papers is herein enclosed under ANNEXE I.

3) I am familiar with above-numbered patent application, with the Official Action of June 18, 2002 and with the cited prior art (i.e. Granger).

4) Granger provides a disclosure of over 1000 different possible combinations of drugs, metals and metal base or basic salts which are intended to confer a cytoprotective effect or reduce the gastrointestinal inflammation.

5) Granger however does not provide any indication about the pharmacokinetics profiles which can be obtained by administering an oral formulation containing one of the possible disclosed combinations.

6) The in vitro dissolution profiles of some of the possible tablet formulations falling within the disclosure made by Granger are compared here-below to that of a tablet formulation according to the present invention.

The compositions and the physical characteristics of the tablet formulations, prepared in laboratory using a single-punch machine equipped with a 7.0 mm convex punch, are given in Tables A and B, respectively.

Table A. Composition of diclofenac potassium matrix tablets obtained by alcoholic granulation (FI → FVI) using a single-punch machine equipped with a 7.0 mm convex punch

Formulation code	Matrix tablet composition (mg and %)																			
	DP[a]		Mannitol		Maize starch		Buffering agent		Methocel A 4C		SLS		Mg stearate		Crospovidone		Macrogol 6,000		Utrawyl		Aerosil P.K. 160	
	mg	%	mg	%	mg	%	mg	%	mg	%	mg	%	mg	%	mg	%	mg	%	mg	%
FI	50.0[a]	32.0	72.0[b]	46.1	25.0	16.0	/		0.2	0.13	0.1	0.06	4.5	2.9	1.0	0.6	/	/	2.5	1.6	1.0	0.6
FII	50.0[a]	32.0	50.0[b]	32.0	25.0	16.0	$KHCO_3$ 22.0[c]	14.1	0.2	0.13	0.1	0.06	4.5	2.9	1.0	0.6	/	/	2.5	1.6	1.0	0.6
FIII	50.0[a]	32.0	62.8[b]	40.2	25.0	16.0	$MgCO_3$ 9.2[c]	5.9	0.2	0.13	0.1	0.06	4.5	2.9	1.0	0.6	/	/	2.5	1.6	1.0	0.6
FIV	50.0[a]	32.0	61.0[b]	39.1	25.0	16.0	$CaCO_3$ 11.0[c]	7.0	0.2	0.13	0.1	0.06	4.5	2.9	1.0	0.6	/	/	2.5	1.6	1.0	0.6
FV	50.0[a]	32.0	65.6[b]	42.0	25.0	16.0	$Mg(OH)_2$ 6.4[c]	4.1	0.2	0.13	0.1	0.06	4.5	2.9	1.0	0.6	/	/	2.5	1.6	1.0	0.6
FVI	50.0[a]	32.0	66.5[b]	42.5	25.0	16.0	$Al(OH)_3$ 5.7[c]	3.6	0.2	0.13	0.1	0.06	4.5	2.9	1.0	0.6	/	/	2.5	1.6	1.0	0.6

DP = Diclofenac potassium
SLS = Sodium lauryl sulphate
[a] Batch no. 9607031 of diclofenac potassium supplied by Irotec (Ireland). Equivalent to 0.15 meq. of hydrochloric acid.
[b] Standard mannitol conform to Eur. Ph..
[c] Equivalent to 0.22 meq. of hydrochloric acid.

Table B. Physical parameters[a] of the diclofenac potassium matrix tablets prepared by alcoholic granulation (FI → FVI), using a single-punch machine equipped with a 7.0 mm convex punch.

Formulation code	Friability[b] (%)	Diameter[c] (mm)	Thickness[c] (mm)	Hardness[c] (N)	Weight (mg)	Disintegration time[d] (min)	Water content[e] (%)
FI	0.6	7.00	3.98	42.7	157.1	5:38	3.7
FII	0.4	7.01	3.64	37.1	157.8	2:32	5.5
FIII	0.6	7.36	3.88	42.20	162.7	3:53	5.3
FIV	0.5	7.37	3.66	48.70	162.5	5:40	4.8
FV	0.4	7.02	3.90	45.80	164.3	5:09	5.5
FVI	1.0	6.97	3.79	37.30	151.6	4:40	5.2

[a] All values are average values determined for six matrix tablets taken at random.
[b] Erweka TA-20 apparatus.
[c] Erweka TBH 30 HD apparatus.
[d] Determined in water (37°C), according to Eur. Ph..
[e] Determined according to Eur. Ph. (Karl Fischer semi-micro water determination).

The unbuffered matrix tablet FI was prepared in laboratory by mixing diclofenac potassium (Irotec batch no. 9607031), standard mannitol (diluent agent) and maize starch (glidant agent), granulating with an ethanolic solution of methocel A 4C (binder) and sodium lauryl sulphate (lubricant agent), then passing the mixture through a no. 0.63 of sieve. The sieved fractions were dried in an oven (35-40°C) for 4 hours. The granules were sieved again (no. 0.8 of sieve) and mixed with magnesium stearate (lubricant agent) for five minutes, then

with crospovidone (binder), ultramyl (disintegrant agent) and aerosil F.K. 160 (disintegrant agent). The granules were compressed (156.3 mg per matrix tablet) on a 7.0 mm convex punch and die using a single-punch machine.

Formulations FII, FIII, FIV, FV and FVI were produced in laboratory by mixing diclofenac potassium (batch no. 9607031, Irotec) with standard mannitol, maize starch and buffering agent, granulating with an ethanolic solution of methocel A 4C and sodium lauryl sulphate, then passing the mixture through a no. 0.63 of sieve. The sieved fractions were dried, sieved again (no. 0.8 of sieve) and mixed with magnesium stearate, crospovidone, ultramyl and aerosil F.K. 160 in a similar manner to formulation FI and the granules were made into matrix tablets as mentioned before for the unbuffered matrix tablets FI.

Dissolution curves for the matrix tablets containing potassium hydrogen carbonate (FII), magnesium carbonate (FIII) and calcium carbonate (FIV) (1.5 meq. per meq. of active ingredient) are depicted in Figure 1 in comparison with that of the control unbuffered matrix tablets FI. In contrast to the unbuffered matrix tablets FI, all the matrix tablets containing carbon dioxide-producing buffering agents gave rapid dissolution of diclofenac potassium. The amount of diclofenac potassium dissolved from the matrix tablets (FII) containing potassium hydrogen carbonate was generally higher than the amount of diclofenac potassium dissolved from matrix tablets (FIII and FIV) containing magnesium and calcium carbonates.

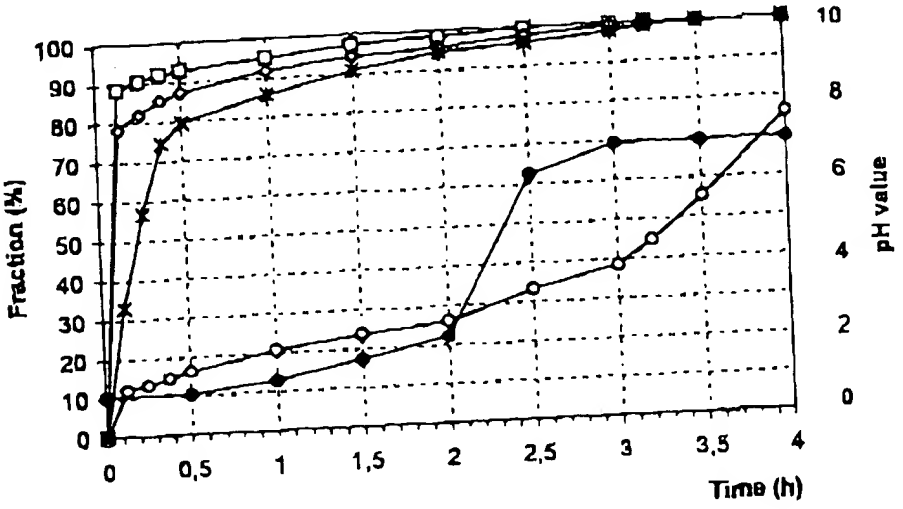


Figure 1. Cumulative fraction of diclofenac potassium released (left y-axis) from the unbuffered matrix tablets FI (○ ○) and the buffered matrix tablets FII (□ □), FIII (◇ ◇) and FIV (✱ ✱) [containing potassium hydrogen carbonate (FII), magnesium carbonate (FIII) and calcium carbonate (FIV) as buffering agents (1.5 meq. per meq. of active ingredient) which produce carbon dioxide in dilute acid] as a function of time at 37°C using a dissolution medium, containing 4% concentration of SLS, where the pH was changed (from about 1 to 7) over a period of 3 hours (stirring rate of 75 rpm). Filled green symbols (● ●) show the time dependence for the pH change (right y-axis).

Dissolution curves for the matrix tablets containing potassium hydrogen carbonate (FII), magnesium hydroxide (FV) and aluminum hydroxide (FVI) (1.5 meq. per meq. of active ingredient) are given in Figure 2 in comparison with that of the unbuffered matrix tablets (FI). The dissolution of diclofenac potassium from the matrix tablets FV and FVI, containing buffering agents insoluble in water but soluble to some extent in dilute acid, was similar to that from the unbuffered tablets FI and much less rapid than that from the matrix tablets FII.

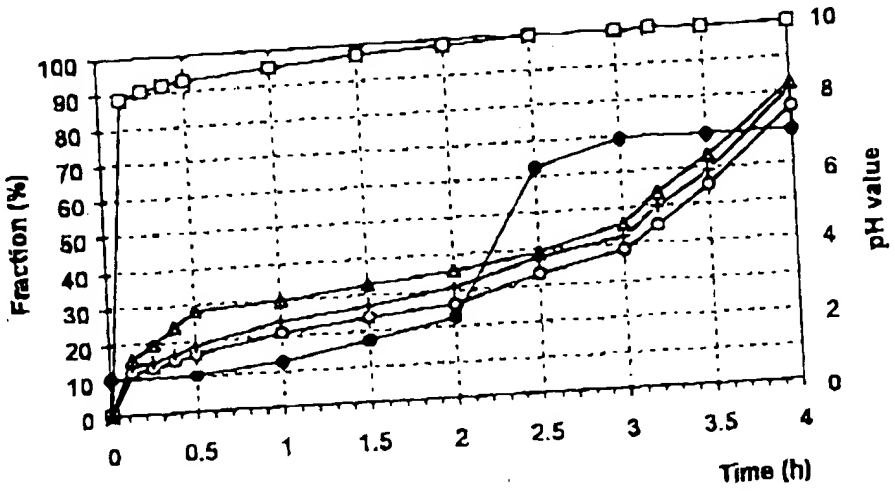


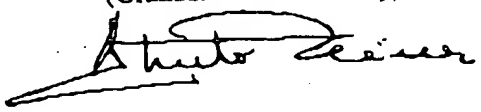
Figure 2. Cumulative fraction of diclofenac potassium released (left y-axis) from the unbuffered matrix tablets FI (○ ●) and the buffered matrix tablets FII (□ ■), FV (+ +) and FVI (△ ▲) [containing potassium hydrogen carbonate (FII) as a buffering agent (1.5 meq. per meq. of active ingredient) which produces carbon dioxide in dilute acid, magnesium hydroxide (FV) and aluminum hydroxide (FVI) as buffering agents (1.5 meq. per meq. of active ingredient) which are insoluble in water but soluble to some extent in dilute acid] as a function of time at 37°C using a dissolution medium, containing 6% concentration of SLS, where the pH was changed (from about 1 to 7) over a period of 3 hours (stirring rate of 75 rpm). Filled green symbols (● ■) show the time dependence for the pH change (right y-axis).

7) From the above-described dissolution tests it can be concluded that a formulation according to the present invention gives a more rapid dissolution of diclofenac than the formulations disclosed by Granger, consequently, we can attend better pharmacokinetics profiles.

8) I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Alberto Reiner
(Graduated in Chemistry)



Date 13 Settembre 2002

CURRICULUM VITAE DEL

DR. ALBERTO REINER

Born in Como (Italy) on April 22, 1938.

Graduated in chemistry at the University of Pavia (Italy) in 1962.

Member of the Italian Chemist Association.

Technical Director of the pharmaceutical firm "Radiumfarm" in Cernusco sul Naviglio (Italy), from 1967 to 1973.

Technical Director of the pharmaceutical firm "Neopharmed" in Baranzate di Bollate (Italy) from 1973 to 1979.

Free lance and consultant for pharmaceutical firms (as for example: Schering, Novartis, Crinos, Pierrel, Knoll-Basf, Recordati, Sigma Tau, Pietro Isnardi, Edmond Pharma, APR, Scharper) since 1980.

President of the pharmaceutical firm "Farmaresa" in Cantù (Italy).

During 2000: the awarding of Lecturer in Regulatory Discipline in post graduate Specialization School at the University of Pavia.

President of the pharmaceutical firm "Farmaresa" in Cantù (Italy)

PATENT PUBLICATIONS NAMING DR. ALBERTO REINER AS INVENTOR

1) "Verfahren zur Herstellung von neuen Stickstoffhaltigen Organischen Verbindungen".
Italian application of: 03/03/64
German patent: n. 252891 of 10/03/67

2) "Verfahren zur Herstellung von neuen Pyridininensalzen der Hydroxy alchilmercaptobuttersauren".
Italian application of: 03/03/64
German patent: n. 247330 of 10/06/66

3) "Composti di N-metil-glucosamina e procedimento per la loro preparazione".
Italian patent application of: 04/09/64; patent granted on: 11/09/67
German patent: n. 251603 of 11/09/67

4) "Composti alogeno alchilati della D glucosamina e procedimento per la loro preparazione".
Italian patent application of: 07/09/64; patent granted on 11/09/67

5) "Sale di lisina ad azione terapeutica".
Italian patent: n. 49557 of 22/04/74

6) "Derivati della piridossina ad attività farmacologica".
Italian application: n. 26327 of 31/07/78

7) "Antiinflammatory and analgesic salicylic acid amide ester(s) - with 2-6-methoxy-2-naphthyl-propionic, 2-4-isobutyl-phenyl-propionic, 4-allyloxy-3-chloro-phenylacetic and similar acids"
PR - 79.03.27 79IT-021320
PN -BE-882480 A 80.07.16 * (8033)
- ZA8001598 A 80.09.02 (8047)
- FR2452479 A 80.11.28 (8104)
- JP55147247 A 80.11.17 (8104)
- US4268685 A 81.05.19 (8123)
- EP--16460 B 82.07.28 (8231) E
- DE3060690 G 82.09.16 (8238)
- CA1134366 A 82.10.26 (8248)

8) "Derivati del paracetamolo ad azione terapeutica, procedimento per la loro preparazione e composizioni farmaceutiche relative".
Italian patent: n. 21321 of 27/03/79

9) "Pyridoxine and isopropylidene-pyridoxine ester(s) of nicotinic acid - with hypoglycaemic and hypocholesterolaemic or analgesic and antiinflammatory activities"
PR - 80.01.22 80IT-019354

- EP--33488 A 81.08.12 * (8134
- JP56104867 A 81.08.20 (8140)
- US4393067 A 83.07.12 (8330)
- CA1173363 A 84.08.28 (8439)
- IT1129707 B 86.06.11 (8745)

10) "Derivati nicotinici di glucosamina, procedimento per la preparazione e relative composizioni farmaceutiche".
Italian application: n. 22188 A/80 of 20/05/80

11) "Lysine salt of 2-thenoyl:thio-propionyl glycine - useful as expectorant, prepd. by reacting stoichiometric amts. of acid and lysine in alcohol solvent
PR - 80.07.22 80IT-023600
PN -- EP--44504 A 82.01.27
- JP57081481 A 82.05.21 (8226)
- IT1148890 B 86.12.03 (8839)

12) "Lysine salt of 2-thenoyl:thio-propionyl glycine - useful as expectorant, prepd. by reacting stoichiometric amts. of acid and lysine in alcohol solvent
PR - 80.07.22 80IT-023600
PN -- EP--44504 A 82.01.27
- JP57081481 A 82.05.21 (8226)
- IT1148890 B 86.12.03 (8839)

13) "Process for preparation of water soluble derivatives of cephalexin".
Italian application: n. 25267 A/80 of 13/10/80

14) "Arginine benzoyl-alpha-mercapto-propionyl glycinate - useful for protecting Liver against toxic conditions"
PR - 80.10.15 80IT-025345
- FR2491925 A 82.04.16 * (8221) 5p
- DE3140847 A 82.05.27 (8222)
- JP57098254 A 82.06.18 (8230)
- IT1195763 B 88.10.27 (9109)

15) "Pyridoxine derivatives, a process for their preparation and related pharmaceutical compositions".
Italian application: n. 2547380 of 21/10/80
European application: n. 81201119.5

16) "Para- isobutyl:phenyl:propionyl thio:ester - of alpha-mercapto:propionyl:glycine, with antiinflammatory and mucolytic activity
PR - 80.11.26 80IT-026232
- JP57167962 A 82.10.16 (8247)
- ES8307733 A 83.11.01 (8406)
- EP--52909 B 85.04.10 (8515) E

- CH-648296 A 85.03.15 (8517)
- DE3169889 G 85.05.15 (8521)
- IT1134457 B 86.08.13 (8803)
- JP89028743 B 89.06.05 (8926)

17) "Para-isobutyl:phenyl:propionyl thio:ester of N-acetyl-cysteine - with antiinflammatory and mucolytic activity"
PR - 80.11.26 80IT-026233
- JP57167963 A 82.10.16 (8247)
- ES8307732 A 83.11.01 (8406)
- EP--52910 B 85.04.10 (8515) E
- CH-648297 A 85.03.15 (8517)
- DE3169890 G 85.05.15 (8521)
- IT1134458 B 86.08.13 (8803)
- JP89028744 B 89.06.05 (8926)

18) "Derivative of N-acetylcysteine having therapeutical activity, process for its preparation and related pharmaceutical compositions".
Italian application: n. 21181 A/81 of 15/04/81

19) "Derivati salicilici di alfa-mercaptopropionilglicina, procedimento per la loro preparazione e relative composizioni farmaceutiche".
Italian application: n. 24843 A/81 of 04/11/81

20) "Tioesteri dell'acido acetilsalicilico, procedimento per la loro preparazione e composizioni farmaceutiche che li contengono".
Italian application: n. 23141 A/82 of 07/09/82

21) "Derivatives of D^2(6 methoxy 2 naphtyl) propionic acid having therapeutical activity, process for their preparation and pharmaceutical compositions containing them".
Italian application: n. 2052383 of 11/04/83
European application: n. 84200478 of 05/04/84

22) "Derivati ad attività terapeutica della S-carbossimetilcisteina, procedimento per la loro preparazione e composizioni farmaceutiche che li contengono".
Italian application: n. 21358 A/83 of 30/05/83

23) "Derivato dell'acido 2-fluoro-alfa-metil-(1-1'-bifenil)-4-acetico ad attività terapeutica, procedimento per la sua preparazione e relative composizioni farmaceutiche".
Italian application: n. 21488 A/83 of 07/06/83

24) "Water-soluble deriv. of 1-hydroxyethyl-2 -methyl-5-nitro-imidazole - having improved activity against trichomonas vaginalis"
PR - 83.06.21 83IT-021704
- AU8429569 A 85.01.03 * (8508) 14p
- JP60013765 A 85.01.24 (8510)

- ZA8404628 A 84.12.21 (8516)
- EP-140395 A 85.05.08 (8519) E
- ES8602690 A 86.03.16 (8620)
- IT1194283 B 88.09.14 (9106)

25) "Novel organic saline derivs. of mercapto:ethane sulphonic acid - are pref. active ingredient of pharmaceutical compsns. for treatment of bladder carcinoma and cistinic kidney calculi"
PR - 85.04.15 85IT-020338
- JP61238722 A 86.10.24 (8649)
- IT1185551 B 87.11.12 (9042)
- EP-198542 B 91.01.02 (9102)
- DE3676335 G 91.02.07 (9107)
- US5019596 A 91.05.28 (9124)
- US5244920 A 93.09.14 (9338) 5p A61K-031/205
- JP2553838 B2 96.11.13 (9650) 5p A61K-031/185
- JP08277262 A 96.10.22 (9701) 6p C07C-323/66
- JP2611949 B2 97.05.21 (9725) 5p C07C-323/66

26) "Derivati salini dell'acido alfa-metil-4-(2 tienil carbonil)-benzen acetico con amminoacidi, procedimento per la loro preparazione e composizioni farmaceutiche che li contengono".
Italian application: n. 20631 A/84 of 19/04/84

27) "Delivery device for constant rate release of therapeutic agent - comprises polymer matrix contg. agent and an additive and two coatings of different polymers"
PR - 84.07.26 84IT-048632
- PT--80865 A 86.01.20 (8608)
- AU8545251 A 86.01.30 (8612)
- NO8502966 A 86.02.17 (8614)
- JP61043109 A 86.03.01 (8615)
- ZA8505553 A 86.01.27 (8619)
- DK8503393 A 86.01.27 (8623)
- FI8502894 A 86.01.27 (8627)
- BR8503539 A 86.04.22 (8630)
- US4681755 A 87.07.21 (8731)
- ES8801123 A 88.03.01 (8816)
- CA1235654 A 88.04.26 (8821)
- IL--75915 A 88.09.30 (8850)
- EP-169821 B 91.02.06 (9106)
- KR-005159 85.07.19

28) "D,L-lysine salt of indomethacin - with improved solubility for treatment of rheumatoid arthritis, gout, spondylitis ankylopoetica and osteoarthritis"
PR - 84.09.06 84IT-048807

- FR2569690 A 86.03.07 (8616)
- AT8502603 A 87.11.15 (8749)
- CH-665832 A 88.06.15 (8828)
- IT1178411 B 87.09.09 (9035)
- DE3531279 C2 94.02.24

29) "New L-carnitine phosphoryl-alkanol-amide cpds. - which are more active than L-carnitine in restoring abnormal lipid metabolism to normal"
PR - 86.01.13 86IT-047524
- JP62190190 A 87.08.20 (8739)
- US4784992 A 88.11.15 (8905) 5p
- EP-232227 B 89.05.31 (8922) E
- DE3760202 G 89.07.06 (8928)
- ES2009856 B 89.10.16 (9003)
- IT1190163 B 88.02.16 (9049)

30) "New aryl-alkanoic acid substd-ethyl ester halide(s) - useful as topical antiinflammatory, analgesic and antiseptic agents"
PR - 86.03.04 86IT-047711
- EP-237495 B 90.09.26 (9039)
- DE3765142 G 90.10.31 (9045)
- ES2017529 B 91.02.16 (9113)
- IT1208736 B 89.07.10 (9135)

31) "Procedimento per la preparazione di derivati salini dell'acido mercapto etan sulfonico". Italian application: n. 21934 A/86 of 08/10/86

32) "Prodn. of antiulcer agents - via new urea and carbodiimide derivs."
PR - 86.11.19 86IT-022389 86.03.28 86IT-019930 87.03.27 87 ES-000878 PN -- WO8705902 A 87.10.08 * (8741) E 26p
- ZA8702271 A 87.09.22 (8801)
- AU8772352 A 87.10.20 (8803)
- EP-269650 A 88.06.08 (8823) E
- FI8705241 A 87.11.27 (8835)
- JP63502903 W 88.10.27 (8849)
- ES2004273 A 88.12.16 (8934)
- IT1198288 B 88.12.21 (9114)
- IT1204495 B 89.03.01 (9126)
- US5030738 A 91.07.09 (9130)
- KR9509825 B1 95.08.29 (9845)

33) "New thioester(s) of ursodesoxycholic acid - useful for treating altered biligenetic function and biliary duct dyskinesia"
DC - B01

PR - 86.11.26 86CH-004728
- US4828763 A 89.05.09 (8922) 2p
- CH-671401 A 89.08.31 (8937)
- EP-273188 B1 92.06.10 (9224) E 6p C07J-031/00
- DE3779740 G 92.07.16 (9230) C07J-031/00
- ES2041671

34) "New ursodeoxycholic acid amide cpds. - of use in the treatment of altered biligenetic functions, lithiasis and dyskinesia"
PR - 86.11.26 86CH-004729
- US4865765 A 89.09.12 (8946) 3p
- CH-674369 A 90.05.31 (9024)
- EP-272462 B1 92.06.10 (9224) E 7p C07J-041/00
- DE3779737 G 92.07.16 (9230) C07J-041/00
- ES2042530 T3 93.12.16 (9403) C07J-041/00

35) "Multi-step prepn. of thioalkyl urea derivs. - esp. ranitidine, niperotidine or cimetidine, which have anti-ulcer activity"
PR - 87.01.27 87IT-019166
PN -- WO8805436 A 88.07.28 * (8831) E 18p
- JP01502026 W 89.07.13 (8934)
- CN1031083 A 89.02.15 (9006)
- IT1215344 B 90.02.08 (9204)
- US5118813 A 92.06.02 (9225) 7p C07D-233/64
- EP-299034 B1
- DE3887019 G 94.02.24 (9409) C07D-407/12
- CA1329615 C 94.05.17 (9425) C07D-233/64
- JP96002865 B2

36) "Phosphorylated derivs. of cpds. with antiinflammatory or analgesic activity - prepd. from ethanol-beta-amino-phosphoric acid, and having low toxicity"
PR - 94.07.22 94IT-MI01555
PN -- EP-693494 A1
- CA2154423 A 96.01.23 (9621) C07F-009/09
- IT1270996 B 97.05.26 (9803) A61K-000/00
- US5849725

37) "Tablet with chewing gum base and contg particles of active ingredient - opt microencapsulated or coated with protective lacquer of cellulose deriv or polyethylene glycol"
PR - 94.07.26 94IT-MI01586
PN -- WO9603111 A1 96.02.08 * (9612) E 17p A61K-009/00
- EP-769935 A1 97.05.02 (9722) E A61K-009/00
- US5711961 A 98.01.27 (9811) 6p A61K-009/68
- IT1274034 B 97.07.14 (9819) A61J-000/00
- CH-689249 A5 99.01.15 (9907) A61K-009/68

38) " Solid oral admin. form giving immediate and sustained release - comprises 1st fraction contg. active agent e.g. ibuprofen in soluble deriv. form giving immediate release, and 2nd fraction contg. same active in non-deriv. form giving sustained release"
PR - 95.06.09 95IT-MI01223
PN -- WO9641617 A1 96.12.27 * (9706) E 37p A61K-009/20
- EP-833618 A1 98.04.08 (9818) E A61K-009/20
- IT1276689 B 97.11.03 (9841) A61K-000/00

39) "Preparazione di nuove formulazioni dietetiche a base di un fosfolipide deacetilato chimicamente isolato allo stato puro".
Italian application: n. MI95001431 of 05.07.1995

40) "Formulazioni per uso topico contenenti carragenina ed un sale dell'acido ialuronico".
Swiss application: n. 02728/95 of 26.09.1995

41) "Nuove composizioni farmaceutiche per uso topico, contenenti iododeossiuridina come principio attivo, e procedimento per la loro preparazione".
Swiss application: n. 03471/95 of 08.12.1995

42) "Nuovi derivati salini della cefalexina e loro composizioni farmaceutiche"
Italian application: n. MI9600183 of 02.02.1996; patent granted on 20.03.1998 (IT-1282376)
Swiss patent application n. 0222/97
Korean patent application n. 3203/1997

43) " Topical compositions containing thermal mud and gelling agent - with active agents for cosmetic or therapeutic treatments
PR - 96.04.24 96CH-001036
- EP-803246 A1

44) "Composition for topical use in the form of gel or cream - contains polysaccharide sulphates with a specified molecular weight, e.g. carrageenins, cosmetics and/or pharmaceuticals, and adjuvants"
PR - 96.11.04 96CH-002719
PN -- WO9819663

45) "Composizioni farmaceutiche contenenti farmaci antiinfiammatori"
Italian application number MI99A002202, dated 99.10.21